REMARKS/ARGUMENTS

The Pending Claims

Claims 1-53 are pending and are directed to a method of increasing the bioavailablility of the active form of *S*-[2-([[1-(2-ethylbutyl)cyclohexyl]carbonyl]amino)phenyl] 2-methylpropanethioate (claims 1-15), a method of increasing the extent of absorption of the active form of *S*-[2-([[1-(2-ethylbutyl)cyclohexyl]carbonyl]amino)phenyl] 2-methylpropanethioate (claims 16-24), a method for decreasing the activity of CETP in a patient (claims 25-33), a method for the treatment of a cardiovascular disorder (claims 34-43), and a kit comprising a pharmaceutical composition comprising *S*-[2-([[1-(2-ethylbutyl)cyclohexyl]carbonyl]amino)phenyl] 2-methylpropanethioate (claims 44-53).

Amendments to the Claims

The claims have been amended to point out more particularly and claim more distinctly the present invention. Claims 1, 16, 25, 34, and 44 have been amended to recite that the pharmaceutical composition is administered to the patient once per day as supported by the specification at, for example, page 8, paragraph 28. Claim 34 has been amended to no longer recite "prophylaxis." Claims 48-50 have been amended to refer to the prescribing information set forth in originally filed claim 44. No new matter has been added by way of these amendments.

Summary of the Office Action

The Office objects to claims 48-50 for allegedly being in improper dependent form. The Office rejects claims 34-43 under 35 U.S.C. § 112, first paragraph, for allegedly lacking enablement.

The Office rejects claims 1-6, 10, 16-21, 25-30, and 34-40 under 35 U.S.C. § 102(b) or 102(e) as allegedly anticipated by either Okamoto et al. (*Nature, 406(13)*: 203-207 (2000)) or Gumkowski et al. (U.S. Patent Application Publication 2006/0014788), respectively. The Office rejects claims 1-10 and 16-43 under 35 U.S.C. § 102(a) as allegedly anticipated by Shinkai et al. I (U.S. Patent 6,426,365).

The Office rejects claims 1-6, 10-21, 25-30, 34-40, and 44-50 under 35 U.S.C. § 103(a) as allegedly unpatentable over Gumkowski et al. in view of Remington's Pharmaceutical Sciences. The Office rejects claims 1-53 under 35 U.S.C. § 103(a) as allegedly unpatentable over Shinkai et al. I in view of Remington's Pharmaceutical Sciences.

The Office rejects claims 1-53 on the grounds of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 1-17 of Shinkai et al. I or claims 1-24 of Shinkai et al. II (U.S. Patent 6,753,346). The Office provisionally rejects claims 1-53 on the grounds of nonstatutory obviousness-type double patenting as allegedly unpatentable over (a) claims 1-18 of co-pending U.S. Patent Application 10/825,531, (b) claims 1-9 and 11-23 of co-pending U.S. Patent Application 10/802,220, or (c) claims 1-5, 7-32, 34-52, and 54-83 of co-pending U.S. Patent Application 10/835,916.

Discussion of the Claim Objection

The Office objects to claims 48-50 for allegedly being in improper dependent form for failing to limit the subject matter of a previous claim. The claims have been amended to refer to the prescribing information set forth in claim 44. As such, the objection to the claims is believed to be moot, and Applicants request that the claim objection be withdrawn.

Discussion of the Enablement Rejection

The Office rejects claims 34-43 for allegedly lacking enablement for the prophylaxis of atherosclerosis or hyperlipidemia. In order to advance prosecution, claim 34 (and, thus, claims 35-43 dependent thereon) has been amended to no longer recite "prophylaxis" as suggested by the Office. Applicants believe that the enablement rejection is moot in view of the amendment and request that the enablement rejection be withdrawn.

Discussion of the Anticipation Rejections

The Office has rejected the claims as allegedly anticipated in view of several references. These rejections are traversed for the following reasons.

1. Okamoto et al.

The Office contends that Okamoto et al. teaches the administration of the claimed compound in the diet of rabbits, which the Office alleges is encompassed by the claims. In Okamoto et al., the compound was added to the rabbits' chow or to a 0.2% cholesterol diet. The pending claims, as amended, require that the claimed compound is administered as part of a pharmaceutical composition once per day. This differs from the disclosure of Okatmoto et al. since the rabbits ingested the compound throughout the day as the rabbits ate the rabbit chow (in typical animal care protocols, rabbits are fed water and food *ad libitum*).

2. Gumkowski et al.

The Office contends that Gumkowski et al. teaches the administration of the claimed compound with soda and ice cream (see paragraph 0112), which the Office alleges is encompassed by the claims. The portion of Gumkowski et al. referenced by the Office is directed to delivery vehicles for an oral formulation comprising a CETP inhibitor. Gumkowski et al. discloses the administration of the oral formulation in soft or hard gelatin capsules or aqueous oral emulsions formed by adding the oral formulation to water or another aqueous liquid (e.g., soda) (see paragraph 0112). Gumkowski et al. also mentions mixing the oral formulation with an aqueous liquid to form a pre-formed emulsion, or adding the oral formulation to food, such as ice cream (see paragraph 0112).

The amounts of additives, such as soda or ice cream, in the delivery vehicles for the oral formulation of Gumkowski et al. would be small and would not be considered to be administration of the oral formulation "with food" as required by the pending claims. The specification of the instant application describes "with food" as referring to the consumption of a solid food with sufficient bulk and fat content that it is not rapidly dissolved and absorbed in the stomach (page 7, paragraph 23). Preferably, the food is a meal, such as breakfast, lunch, or dinner. Indeed, the Examples demonstrate the administration of the pharmaceutical composition of the invention after a meal (i.e., in the fed state) (see page 12, paragraph 47, and pages 12-13, paragraphs 50-51). The minor amounts of soda or ice cream formulated in an oral dosage form as described by Gumkowski et al. would not meet the requirements of the definition of "food" in the specification.

Indeed, Gumkowski et al. is directed to oral formulations of CETP inhibitors that improve exposure of the CETP inhibitors in the *fasted* state (see paragraph 0013). Gumkowski et al. teaches away from administering CETP inhibitors with food because dependence on exposure of food could compromise the effectiveness of the medication due to a lack of patient compliance with labeling instructions (see paragraph 0012), thereby leading to patient-to-patient variability in treatment (see paragraph 0013).

Moreover, while Gumkowski et al. discloses that the blood levels of *some* CETP inhibitors, when administered with triglyceride solutions, are affected by food (see paragraph 0012), Gumkowski et al. does not disclose whether the particular compound recited in the pending claims in combination with triglyceride solutions is affected by administration with food. The compound recited in the pending claims is only disclosed in an extensive list of CETP inhibitors that can be used in the oral formulation of Gumkowski et al. (see paragraphs 0113-1035), which oral formulation is designed to improve exposure of a CETP inhibitor in the *fasted* state as described above (see paragraph 0013).

3. Shinkai et al. I

The Office contends that, while Shinkai et al. I does not expressly teach that the compound is administered with food, ingredients in the tablets or capsules, such as lactose and starch, allegedly qualify as foods, such that Shinkai et al. I anticipates the claims.

As discussed above, the specification describes "with food" as referring to the consumption of a solid food with sufficient bulk and fat content that it is not rapidly dissolved and absorbed in the stomach (page 7, paragraph 23). Preferably, the food is a meal, such as breakfast, lunch, or dinner. Indeed, the Examples demonstrate the administration of the pharmaceutical composition of the invention after a meal (i.e., in the fed state) (see page 12, paragraph 47, and pages 12-13, paragraphs 50-51). The minor amounts of lactose or starch formulated in an oral dosage form do not meet the requirements of the definition of "food" in the specification. Furthermore, one of ordinary skill in the art would not categorize such non-active ingredients in an oral dosage form as "food."

For the above reasons, the cited references cannot be considered to anticipate the pending claims, and the anticipation rejections should be withdrawn.

Discussion of the Obviousness Rejections

The Office rejects the claims as allegedly obvious in view of Gumkowski et al. or Shinkai et al. I for those reasons discussed above corresponding to the anticipation rejections and further in view of Remington's Pharmaceutical Sciences. The Office concedes that Gumkowski et al. and Shinkai et al. I do not disclose providing the composition to a patient in a container associated with prescribing information (such as a kit), but the Office contends that Remington's Pharmaceutical Sciences discloses labeling instructions (e.g., for a kit). The Office also concedes that Gumkowski et al. and Shinkai et al. I do not disclose the dosages recited in claims 2, 3, 17, 18, 26, 27, 36, and 37, but the Office contends that it would be within the skill of an ordinary artisan to discover optimum or working ranges by routine experimentation. Applicants traverse these rejections for the following reasons.

As discussed above, Gumkowski et al. is directed to oral formulations of CETP inhibitors that improve exposure of the CETP inhibitors in the *fasted* state. Gumkowski et al. teaches away from administering CETP inhibitors with food because dependence on exposure of food could compromise the effectiveness of the medication due to a lack of patient compliance with labeling instructions, thereby leading to patient-to-patient variability in treatment.

Similarly, as discussed above, one of ordinary skill in the art would *not* recognize the routine formulation of oral dosage forms with additives, such as lactose and starch as disclosed by Shinkai et al. I, as administration of a CETP inhibitor (such as the compound recited in the pending claims) "with food" as required by the pending claims.

Therefore, even with the addition of Remington's Pharmaceutical Sciences, one of ordinary skill in the art would not arrive at the invention of the pending claims, which claims require the administration of a pharmaceutical composition with food once per day. Thus, the cited references, whether considered alone or together, cannot be considered to render obvious the subject matter of the pending claims, and the obviousness rejections should be withdrawn.

Discussion of the Obviousness-type Double Patenting Rejections

The Office has rejected the claims for obviousness-type double patenting in view of several references. These rejections are traversed for the following reasons.

1. Shinkai et al. I, Shinkai et al. II, or U.S. Patent Application 10/825,531

Shinkai et al. I and co-pending U.S. Patent Application 10/825,531 ("the '531 application") contain claims directed to a compound that encompasses the species of the compound recited in the pending claims. Shinkai et al. I contains only compound claims. The '531 application contains compound claims, composition claims, and method claims (specifically, a method for inhibition of CETP activity, a method for the prevention or therapy of hyperlipidemia, and a method for the prevention or therapy of atherosclerosis).

Shinkai et al. II contains claims directed to *S*-[2-([[1-(2-ethylbutyl)cyclohexyl]carbonyl]amino)phenyl] 2-methylpropanethioate, as well as a method of inhibiting CETP activity, a method of increasing HDL, a method of decreasing LDL, a method of treating or preventing atherosclerosis, and a method of treating or preventing hyperlipidemia.

The claims of the cited references do not teach or suggest administering *S*-[2-([[1-(2-ethylbutyl)cyclohexyl]carbonyl]amino)phenyl] 2-methylpropanethioate with food, as recited in the pending claims.

Accordingly, the subject matter of the pending claims cannot be considered obvious in view of the claims of the cited references, and the obviousness-type double patenting rejections based on the foregoing references should be withdrawn.

2. U.S. Patent Application 10/802,220 or U.S. Patent Application 10/835,916

The obviousness-type double patenting rejections based on these references are "provisional," and Applicants will address the rejections at which time the cited applications issue as patents and the rejections become non-provisional.

Conclusion

Applicants respectfully submit that the patent application is in condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,

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